REMARKS

The application is amended to correct various typographical, grammatical and idiomatic informalities, and to place the application into proper conformance with U.S. patent practice.

The abstract is replaced to ensure conformance with U.S. filing requirements.

It is respectfully requested that the first Office Action be directed to the application as amended herein. Please charge any fee deficiency or credit any excess payment to Deposit Account No. 10-1250.

Respectfully submitted,

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TITLE OF THE INVENTION

[Bio-decomposable polymer composition showing good thermal decomposition]

BIODEGRADABLE POLYMER COMPOSITION SHOWING GOOD RESISTANCE TO THERMAL DECOMPOSITION

BACKGROUND [of] OF THE INVENTION

1. Field of The Invention

This invention relates to [bio-decomposable] a biodegradable polymer composition [showing] that exhibits good resistance to thermal decomposition, [in which a drop of] resulting from molding or radiation sterilization. It has been found that it is possible to control the reduction in weight-average molecular [is possible to control] weight caused by thermal decomposition to within 30 % of the initial molecular weight after [treatment of] molding and [radial] radiation sterilization, by adding a free radical scavenger to the [bio-decomposable] biodegradable polymer.

In this invention, the [bio-decomposable] biodegradable polymer [is defined as a gentle polymer for organ and] has sufficiently mild properties so that it is suitable for medical treatment of parts of the body and their environment, [after] while maintaining [for a certain] its shape and properties for a necessary period [certain shapes and properties both out- and inside organs, hydrolyzing by] . After

such treatment, the polymer may be caused to disappear by hydrolyzing with an enzyme or non-enzyme [and disappearing the shapes].

2. Description of The Related Art

The [bio-decomposable] biodegradable polymer [is composed of] may be natural [and] or synthetic [polymers], and an enzyme [hydrolyzes] is capable of hydrolyzing almost all natural polymers[, in which a] . For example, collagen [composed of] which is a polypeptide, is [a] representative of the natural [polymer] polymers and is hydrolyzed by [collagenaze. And] collagenase, while a polyglycoside [composing] composed of [glycoside combination, is mentioned] combined glycosides such as cellulose, starch, hyaluromic acid, chitin and chitosan is also contemplated[. The] , with cellulose [is also] , for example being hydrolyzed by [cellulaze] cellulase enzyme.

In spite of [a] the fact that a natural polyester produced by a microbe was known as a [bio-decomposable] biodegradable polymer since 1920 [years, but] , such knowledge was not [applied] utilized for a long time. However, as a result of [nowadays] recent progress in [bio-technology] biotechnology, many kinds of natural polyesters [are] have been researched and developed as [bio-decomposable] biodegradable materials, including [of poly- β - hydroxy butylate] poly β-hydroxybutylate.

[On the other hand, many] Many kinds of synthetic [bio-decomposable] biodegradable polymers [belong to such polymer scopes hydrolyzing by] are capable of being hydrolyzed by a non-enzyme[, however] . However, [polypeptide] polypeptides such as poly glutamic acid [is] are hydrolyzed by peptide decomposition [enzyme] enzymes similar to natural [poly-peptide] polypeptides.

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Almost all biodegradable synthetic [polyester of the bio-decomposable polymers belong to] polyesters such [polymers] as [poly-glycolic] polyglucolic acid, [poly-lactic] polylactic acid or [co-polymer] copolymers of glycolic and lactic acids, [hydrolyzing] are hydrolyzed by [non-enzyme] non-enzymes and [frequently applying in] find frequent clinical use as medical materials[, today].

There are many medical applications of [the bio-decomposable] biodegradable polymers [employing] employed as medical materials, but [restricting within] these are almost always restricted to surgical use [of clinical field] such as suture [of operation] or bone fixation materials. [There are employed as many other] Other industrial uses [including] of these polymers include PLLA film molded products such as a garbage [bag] bags, agricultural film, [stored bag] storage bags, or textiles, [as] since PLLA is [possible to be] decomposed by [a microbe] microbes under [nature] a natural environment.

[On the other hand, produced method of bio-decomposable polymer is applied by such as production] The production of biodegradable polymers useful as medical and industrial materials is accomplished by such methods as extrusion of heated meltdown, injection, and pressed molding [in common use as medical and industrial materials]. However, heating [process is inevitably] processes are usually avoided in [record] the course of production[.

B2

But] , since a drop [of] in molecular weight inevitably [happens] occurs in products after such heating process, because [bio-decomposable polymer] biodegradable polymers generally [shows] have poor heat stability. In addition, sterilization is inevitably necessary [different from the] for medical use in contrast with industrial use, because [bio-decomposable polymer is] biodegradable polymers are applied in surgical use [of clinical field] such as [suture of operation] surgical sutures or bone fixation materials. Ethylene-oxide gas is generally [applied] utilized for the sterilization process, because [bio-decomposable polymers shows] biodegradable polymers show poor durability against radiation exposure. [But in] In this process, since ethylene-oxide gas [applied] utilized for the sterilization, is intended to eliminate toxicity in the living body, [therefore,] it is inevitably necessary to remove residual gas after the sterilization process, by [sucking up long time] applying vacuum for an extended period [in order to remove the gas], but it is nevertheless impossible to [perfectly] completely remove the gas. [Present

sterilization method] Sterilization methods by radiation [irradiation is] are therefore employed in many cases [of bio-decomposable] when biodegradable polymers [applied in] are utilized for medical [use category as a result. And] uses. Moreover, only specified kinds of [bio-decomposable] biodegradable polymers are [possibly] generally irradiated, but some strength deterioration inevitably [avoids] occurs, caused [on] by radiation decomposition [by irradiation].

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It is the object of this invention to treat biodegradable polymers so as to avoid or restrict molecular weight [drop] reduction in the course of heat treatment [process] processes, and strength deterioration, caused by sterilization, and [fabricating polymer] to improve the properties of the composition [by applying the restricted] containing the treated polymer.

SUMMARY [of] OF THE INVENTION

In this invention, [after wholeheartedly investigation, we propose bio-decomposable] the production of a biodegradable polymer composition showing good resistance to thermal decomposition, wherein a drop of weight-average molecular weight is controlled [controls] within 30 % of the initial molecular weight after [treatment of] molding and [radial] radiation sterilization process, is accomplished by adding a free radical scavenger to the [bio-decomposable] biodegradable polymer, [in order to resolve the above problem].

[Bio-decomposable] Biodegradable polymer [composition] compositions of the invention, [standing] notwithstanding thermal and [radial decompositions] radiation decomposition, [is possibly applied] are applicable for medical and many [other] industrial uses. Moreover, this processing method [is] may be applied [for non-bio-decomposable polymer fields] to non-biodegradable polymers such as nylon or polypropylene [for sterilization of] when subjected to thermal casting and sterilization by irradiation.

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DETAILED DESCRIPTION [of] OF THE INVENTION

For [bio-decomposable] treatment of the biodegradable polymer [composition] compositions of the invention, the free radical scavenger is selected from the [oxidizing resistance] oxidation resistant agent group consisting of polyphenols, tannic acids, or gallic acids, the vitamin group consisting of Vitamin E or Vitamin C, or triarylisocianulate, [by adding the] such free radical scavenger being added to [bio-decomposable] the biodegradable polymer composition, to improve its properties after thermal, mechanical and irradiation [improve properties] treatments.

When the [bio-decomposable] biodegradable polymer is heated [up] until [50-degree] its temperature is 50-degrees Centigrade higher than its melting temperature, radicals [generate] are generated from the polymer. Moreover, the

polymer begins to [be deteriorated] deteriorate by an oxidizing reaction caused by ambient oxygen. The molecular weight of the polymer is [intensely deteriorated by] substantially reduced by a high dose (of 2 to 3 MRad) applied radiation similar in effect to heating, generating radicals in molecular chains of the polymer, [cutting] causing breaks in the chains and [intensely deteriorating] substantially reducing the molecular weight.

B2

[Here, in] In order to prevent the molecular chains from [cutting] being broken by the generated radicals [caused by thermal] as a result of heating and irradiation, [we can attain our goal, by previously adding] the free radical scavenger [to bio-decomposable] can be previously added to the polymer composition in order to [catch] inactivate the generated radicals[,].

[Additional] The volume of the free radical scavenger added to the composition is preferably [a] in the range of 0.01 to 10wt.%, more preferably a range of 0.01 to 2wt.%, [for 100 wt.%] based on the weight of the polymer. If the [additional] volume of scavenger is less than 0.01 wt.%, [it will take many hours before we get] the time necessary to obtain desired results will be undesirably long. If [additional] volume is more than 10wt.%, the [addition does not have any effect on, but obstruction to] added scavenger may have a negative rather a positive effect on the molecular weight of the polymer.

There is no special method or process for adding and mixing free radical scavenger [to] with the [bio-decomposable] biodegradable polymer composition. For example, [in a case of] when adding vitamin E, it is possible not only to [direct adding] directly add the vitamin E to the polymer in the mentioned volume range, but also at first [mixing] mix and [solving] dissolve the vitamin E in an organic solvent such as acetone, [making] causing a mixture of the polymer and vitamin E [by adding and mixing,] to remain at final drying [up] of the [mixture] resulting solution.

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In order to [get uniform] obtain additional uniform mixture, the [bio-decomposable] biodegradable polymer composition [is possibly] may be absorbed [and formed] to form a complex [in] with an inorganic [compounds] compound such as apatite, zeolite or titanium dioxide.

[Heat-treat methods] Operations involving the application of heat including extrusion, injection and heat pressing [are pointed out, as a] may be part of the manufacturing process [of the bio-decomposable] for producing a biodegradable polymer composition [of] by adding and mixing a free radical scavenger with the polymer. It is preferred that the composition is produced at [not] a temperature not more than 50-degree Centigrade higher than the melting temperature of the [bio-decomposable] biodegradable polymer, because [its] such temperature is the upper limited temperature for generating free radicals. There is no restriction with

respect to [under limited] a lower limit of the temperature for generating free radicals, but it is preferred to produce [at] such radicals at a higher temperature than the softening point of the [bio-decomposable] biodegradable polymer because of [view of easy] greater ease of production.

The [bio-decomposable] biodegradable polymer composition [previously] prepared by adding and mixing the free radical scavenger with the polymer is [irradiated] sterilized with radiation such as ^{60}C o - γ ray [and sterilized, applying] by [ordinary] a conventional method. It is preferred that the radiation is [irradiated and] produced in a dose range of 1.0 to 3.0Mrad. [It is not preferred that if] If the radiation is [irradiated] less than 1.0 Mrad dose, [sterilized] the sterilization effect is poor, and if more than 3.0 Mrad dose, the molecular weight of the polymer begins to deteriorate.

There is no special [rule] procedure for [produced] carrying out the steps [of] involving heating [process] and [sterilized process irradiating] radiation sterilization. [But] However, it is preferred that [at first step,] the heating step [process] is carried out first, [and next, sterilized process are performed in order to easily produce] because of greater ease of production.

The [bio-decomposable] biodegradable polymer of this invention is composed of any of natural and synthetic polymers, and free radicals [happen] are generated during [produced] steps of heating [process] and [sterilizing process by

irradiated] radiation sterilization. The [, in which the] polymer includes, for example any of the group consisting of poly-glycolic acid, poly-lactic acid, poly-dioxanon, gelatin, hyaluronic acid, collagen, poly-amino acid, poly-caprolacton, copolymer of lactic and glycolic acid, copolymer of lactic acid and caprolacton, copolymer of glycolic acid and caprolactone, poly-hydroxybutylate, chitin, albumin, or chitosan. [Bio-decomposable] The biodegradable polymer composition of the invention is [possibly applied] applicable for medical and many [other] industrial uses.

By this invention, the [bio-decomposable] biodegradable polymer is prevented from an occurrence of molecular weight loss [from degrading in produced steps of] caused by heating [process] and [sterilizing process] by [irradiated] radiation[. The] sterilization. This results in the production of high quality [bio-decomposable] polymer [composition] compositions [is possibly produced].

In conclusion, products of [bio-decomposable] biodegradable polymer [composition] compositions produced by this invention such as [suture] sutures for [operation] operations and bone fixation material [are maintained] maintain their mechanical properties[, prevented] and have other improved properties due to the prevention of molecular weight loss [from deteriorating and improved several

properties,] caused [of] by heating [process and sterilizing process by irradiated] and radiation sterilization.

Other [polymer materials] polymers which may be added to the [bio-decomposable] biodegradable polymer, such as polyethylene for artificial joint friction parts, that [needs] require heating [process] and [sterilizing process by irradiated] radiation sterilization, can [be applied] also be treated by this invented method, in order to prevent molecular weight loss from [deteriorating] accelerating.

[EXAMPLE] EXAMPLES

[Followed] The following examples [show detailed explanation of this] illustrate the invention, [however the invention is not restricted by the examples] but do not restrict the scope of such invention as claimed herein.

The weight-average molecular weights shown in the examples are measured by Shimazu GPC.

Example 1

[After we made about 340 thousand] To poly-L-lactide(PLLA) [material of] having a weight-average molecular [by adding] weight of 340 thousand was added 0.1 wt.% Vitamin E(Tocopherol)[, and] . From this composition, a molded rod

sample of 10cm length and 10mm diameter [by] was formed using an injection machine (Nisshou Jushi Ind. Ltd., NS40-A).

While the weight-average molecular weight of the PLLA rod having no Vitamin E additive declined [until] to about 180 thousand after molding, the weight-average molecular weight of PLLA rod having Vitamin E additive showed almost no molecular weight drop [of] , at about a 330 thousand molecular weight.

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Example 2

[We spun the thread of] To PLLA [pellet by applying simplified melting spinner that PLLA showed its] having a weight-average molecular weight of about 280 thousand [and] was added 1.0 wt. % of Vitamin E. Pellets of this composition were spun into thread using a simplified melt spinner. The molecular weight after spinning [showed] was about [26] 260 thousand, indicating a small molecular weight [drops] drop.

[On the other hand] In contrast, PLLA thread [adding] similarly spun but with no Vitamin E additive [declined until] had a reduced molecular weight of about 140 thousand, about half the molecular weight of [initial product] the Vitamin E-containing PLLA after spinning

Example 3

PLLA [pellet] pellets of weight-average molecular weight of about 280 thousand [was made to] were modified by treated samples [composing] composed of 100 parts of titanium dioxide (WakoJunyaku Co.) and 10 parts of tannin (WakoJunyaku Co.) that was absorbed in the titanium dioxide. [Next, we fabricated] A PLLA rod [by adding] was then fabricated from polymer pellets containing 0.5 parts of treated samples per tannin unit [to the PLLA pellet].

The molecular weight after molding the rod [showed] was about [26] 260 thousand, indicating [relative] a relatively small molecular weight [drops] drop, while the molecular weight of the PLLA rod having no tannin additive declined [until] to about 140 thousand.

Example 4

[Copolymer] To a copolymer of L-lactide(75 mol%) and caprolactone (25 mol%) [of] having a weight-average molecular weight of about 340 thousand was [made], added Vitamin E in the amount of 0.2 wt.% and [spun the] the copolymer was used to spin thread [by applying by] with a simplified [melting] melt spinner. [Weight-average] The weight-average molecular weight of the copolymer was about 330 thousand and indicated a small molecular weight [drops] drop from that of the copolymer containing no Vitamin E.

Example 5

[Melt-spun] The melt-spun thread [gotten by] of Example 4 was packed in a bag laminated [by] with aluminum and polyethylene film [and] , the air in the bag was replaced by nitrogen gas, and the thread was irradiated [and exposed] by exposure to radial ray (^{60} C o - γ ray) of 2.5 Mrad. [Weight-average] The weight-average molecular weight of the thread after radiation was about 300 thousand.

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Example 6

To PLLA [pellet] pellets of weight-average molecular weight of about 280 thousand was added triarylisocianulate in an amount of 0.2 wt.%, and the composition was extruded to a rod [shape] of 2 mm diameter [by extruder. Weight-average] . The weight-average molecular weight of the extruded PLLA was slightly increased [until] to 290 thousand.

[Further, we made the] The product [vacuum-packing] was vacuum-packed and [irradiating] irradiated, [exposing] by exposure [by] to radial ray (^{60} C o - γ ray) of 2.0 Mrad, [and getting] to obtain a cross-linked product [that showed] having improved mechanical properties [improved].

Example 7

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[At first, we fabricated] A treated specimen was prepared composed of 100 parts hydroxy-apatite and 1 part Vitamin E absorbed in the hydroxy-apatite. A mixture composed of 100 parts of PLLA [pellet] pellets of weight-average molecular weight of about 280 thousand was mixed with 30 parts of the treated specimen in apatite and molded by injector. [Molecular] The molecular weight of PPLA in [obtained] the resulting composite [showed almost no molecular weight drop of] was about 330 thousand [molecular weight]. After forming the composite by [applying] means of a hydrostatic pressure type extruder in order to orientate the molecular chains, the composite was irradiated [by] with ^{60}C o - γ radiation of 2.5MRad [and] to obtain the finished PLLA/apatite composite which had a molecular [. Molecular] weight [and] of about 300 thousand and superior mechanical properties [of the composite showed about 300 thousand] , for example, high tenacity and high modulus[, respectively].

Abstract

[Bio-decomposable] A biodegradable polymer composition [shows] having good resistance to thermal decomposition, wherein [a drop of] it is possible to control the weight-average molecular [controls] weight to within 30 % of the initial molecular weight after [treatment of] molding and [radial] radiation sterilization, by adding a free radical scavenger to the [bio-decomposable] biodegradable polymer[, in order to resolve the problem].

[Bio-decomposable] Biodegradable polymer [composition] compositions of the invention, [standing] which withstand thermal and [radial decompositions is possibly applied] radiation decomposition are effective for medical and many [other] industrial uses. Moreover, this [processing] inventive method is [applied] applicable for [non-bio-decomposable polymer fields] the treatment of many non-biodegradable polymers such as nylon or polypropylene [for sterilization of] which are subjected to thermal casting and [irradiation] radiation sterilization.